DOW CORNING

8EHQ-0896-13709S

August 6, 1996

SANITIZED VERSION

TSCA Document Processing Center (7407)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Attn: TSCA Section 8(e) Coordinator
401 M Street S.W.
Washington, D.C. 20460

8EHQ-96-13709
88960000 1895

Re: TSCA Section 8(e) Notification of Substantial Risk
Hydroxy-terminated [3-(2-aminoethyl)amino]propyl Me silsesquioxanes

Dear Sir:

In accordance with the provisions of Section 8(e) of the Toxic Substances and Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (40 FR 11110, March 16, 1978), Dow Corning is submitting the following information as a Notification of Substantial Risk for a recently completed study.

Chemical Substance:

The test substance, [CONFIDENTIAL], has the following chemical composition:

CASRN	WEIGHT		CHEMICAL NAME
67-56-1	1	Imp	Methanol
7732-18-5	97		Water
PMN-94-2233	2		Silsesquioxanes, [3-(2-aminoethyl)amino]propyl Me, hydroxy-terminated

Manufacturer:

Dow Corning Corporation
2200 West Salzburg Road
Midland, Michigan 48686-0994

Recently Completed Study:

SKIN SENSITIZATION STUDY OF [CONFIDENTIAL] USING THE GUINEA PIG MAXIMIZATION TEST (GMT)

Dow Corning Corporation
1996-I0000-41490
July 19, 1996

Executive Summary:

A guinea pig sensitization assay was conducted to determine the dermal sensitization potential of [CONFIDENTIAL]. This study was performed according to the OECD Guidelines No. 406 (July, 1992) and US EPA Good Laboratory Practice Standards Part 792 (TSCA), 40 CFR 792, Final Rule, August, 1989. The test substance was administered by intradermal (i.d.) injection of the dosing formulation (5% w/v) in saline to the shaved shoulder region of 20 male guinea pigs. Another group of 10 male vehicle control guinea pigs was handled in a similar manner, but were treated (i.d.) with saline only. A third group of 10 male guinea pigs was treated with dinitrochlorobenzene (DNCB) in propylene glycol and served as a positive control. One week following injection of the first induction dose, a second induction dose (100%) of the test substance was applied topically to the test group animals for 48 hours. Animals in the vehicle control and positive control groups were dosed topically with saline and DNCB, respectively. Three weeks following the first induction dose, test and vehicle control guinea pigs received a topical challenge (75% w/v) of [CONFIDENTIAL]/saline vehicle formulation for 24 hours. Positive control guinea pigs were dosed similarly with DNCB in propylene glycol. A second challenge dose of test substance/saline formulation was administered to test and vehicle control animals one week following the first challenge dose. The skin response of all guinea pigs was evaluated at approximately 24 and 48 hours following completion of each challenge dose. The results were expressed in terms of the incidence and severity of the skin response.

All the positive control animals exhibited a positive reaction at the DNCB challenge control site. The combined (24 and 48 hour) positive response resulted in 32 of 40 (80%) test substance-treated animals being sensitized by the test material, based on the presence of erythema at the challenge site.

TSCA CBI Waiver:

For purposes of notification of substantial risk under TSCA Section 8(e), the general PROPRIETARY designation on the attached toxicological study has been waived by Dow Corning. Only the trade name of the test substance, but not its chemical identity, has been claimed as confidential business information.

Actions:

Dow Corning will inform the Agency of any pertinent information that may be developed concerning this material.

If you have any questions concerning this study, please contact Dr. Waheed Siddiqui, Associate Toxicology Scientist, Product Safety and Toxicology Department, at 517-496-4884 or at the address provided herein. If you require further general information regarding this submission, please contact Dr. Rhys G. Daniels, Regulatory

Compliance Specialist, Product Stewardship and Regulatory Compliance Department, at 517-496-4222 or at the address provided herein.

Sincerely,

Michael P. Hill
U.S. Area Vice President
Director of Health and Environmental Sciences
(517) 496-4059

RGL 96160

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

IIT RESEARCH INSTITUTE
LIFE SCIENCES DEPARTMENT
10 W. 35TH STREET
CHICAGO, IL 60616

Report No: 1996-I0000-41490

Title SKIN SENSITIZATION STUDY OF [ ] USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

Study No: 8432

External Testing Facility No: L08573-13

Test Substance: [ ]

Study Director: John Findlay, B.S.
Research Toxicologist

Author: John Findlay, B.S.
Research Toxicologist
J. Fred Krueger, M.S.
Sr. Technical Editor

Sponsor: Dow Corning Corporation
2200 W. Salzburg Road
Midland, MI 48686-0994

Sponsor Representative: Waheed Siddiqui, Ph.D.
Associate Toxicology Scientist

Testing Facility: IIT Research Institute
Life Sciences Department
10 West 35th Street
Chicago, IL 60616-3799

Study Completion Date: May 1996

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ABSTRACT

The purpose of this study was to determine the dermal sensitization potential of[ ]n guinea pigs using the Guinea Pig Maximization Test (GPMT).

[ ]was administered by intradermal (i.d.) injection of dosing formulation in saline to the shaved shoulder region of twenty male guinea pigs. Another group of ten male vehicle control guinea pigs was handled in a similar manner, but was treated (i.d.) with saline only. A third group of ten male guinea pigs was treated (i.d.) with DNCB in propylene glycol and served as a positive control. One week following injection of the first induction dose, a second induction dose of test substance was applied topically to the test group for 48 hours. Animals in the vehicle control and positive control groups were dosed (topical application) with saline and DNCB, respectively. Three weeks following the first induction dose, test and vehicle control guinea pigs received a topical challenge dose of test substance/saline formulation for 24 hours. Positive control guinea pigs were similarly dosed with DNCB in propylene glycol. A second challenge dose of test substance/saline formulation was administered to test and vehicle control animals one week following the first challenge dose. All guinea pigs were scored for erythema and edema according to the Draize scale approximately 24 and 48 hours following completion of each challenge dose. The results of the challenge were expressed in terms of the incidence and severity of the skin response, with an erythema and/or edema score of 1 or greater being considered a positive response. This study was performed using OECD Guidelines for Testing of Chemicals (Part 406, July, 1992) and according to U.S. EPA Good Laboratory Practice Standards set forth in Part 792 (TSCA) of Title 40 of the *Code of Federal Regulations*, Final Rule, August 17, 1989.

All of the positive control animals exhibited a positive reaction at the DNCB challenge site. The combined (24 and 48 hour) score resulted in thirty two (32) out of 40 (80%) test substance-treated animals exhibiting a positive reaction following the second challenge. Therefore, according to the modified scoring rating of Kligman (Kligman, A.M., *J. Invest. Dermatology*, 1966)[ ]s considered a strong skin sensitizer in guinea pigs.

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GLP COMPLIANCE STATEMENT

This study was conducted in accordance with U.S. Environmental Protection Agency (EPA) TSCA Good Laboratory Practice (GLP) Standards as set forth in the *Code of Federal Regulations* (Part 792 Title 40), except that no analyses were performed to determine the concentration, homogeneity and stability of the dosing formulations. Records pertaining to the characterization of the bulk test substance were the responsibility of the Sponsor and are maintained at the address indicated for the Sponsor. The raw data have been reviewed by the Study Director, who certifies that the information contained in this report is consistent with and supported by the study raw data.

John Findlay 5/30/96

John Findlay, B.S. Date
Study Director
Life Sciences Department

QUALITY ASSURANCE STATEMENT

Study Title: Skin Sensitization Study of[ ]sing the in the Guinea Pig Maximization Test (GPMT)

Project Number: L08573

Study No.: 13

Study Director: John Findlay, B.S.

This study has been subjected to inspections and the report has been audited by the IITRI Quality Assurance Unit in accordance with U.S. Environmental Protection Agency (EPA) TSCA "Good Laboratory Practice (GLP) Standards" - "CFR Title 40 Section 792.35". The report describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

The following are the inspection dates and the dates inspection findings were reported:

		Findings Reported To:	
Date of Inspection	Study Phase	Study Director	Management
October 18, 1995	Protocol review	October 18, 1995	October 18, 1995
November 7, 1995	Rangefinding test substance administration	November 7, 1995	November 7, 1995
November 9, 1995	Protocol review	November 9, 1995	November 9, 1995
November 21, 1995	Protocol amendment review	November 21, 1995	November 21, 1995
November 21, 1995	Test and control substance prep	November 21, 1995	November 21, 1995
December 12, 1995	Test and control substance prep	December 12, 1995	December 12, 1995
December 19, 1995	Test substance administration	December 19, 1995	December 19, 1995
February 6, 7, 1996	Report/data audit	February 7, 1996	February 7, 1996

R. A. Boyne 5/29/96

Ronald A. Boyne, B.S. Date
Manager, Quality Assurance

APPROVAL SIGNATURES

This report consists of Pages 1 through 22 including Tables 1 through 2 and Appendices 1 through 3.

John Findlay — 5/30/96
Date

John Findlay, B.S.
Research Toxicologist
Life Sciences Department
Study Director

David McCormick — 5/30/96
Date

David McCormick, Ph.D., D.A.B.T.
Manager, Toxicology and Carcinogenesis
Life Sciences Department

W Siddiqui — 5/17/96
Date

Waheed Siddiqui, Ph.D.
Associate Toxicology Scientist
Sponsor Representative

STUDY INFORMATION

Study Initiation Date:	November 7, 1995
Experimental Start Date:	November 21, 1995
Experimental Termination Date:	December 22, 1995
Study Director:	John Findlay, B.S.
Sponsor:	Dow Corning Corporation
Sponsor Representative:	Waheed Siddiqui, Ph.D.
Study Personnel:	Lucy Touma-Youakim, M.S., Laboratory Toxicologist Melissa Luther, B.S., Laboratory Toxicologist
Report Preparation:	J. Fred Krueger, M.S., Senior Technical Editor

SKIN SENSITIZATION STUDY OF[ ]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

I. INTRODUCTION

The purpose of this study was to determine the dermal sensitization potential of[ ]in guinea pigs using the Guinea Pig Maximization Test (GPMT).

II. MATERIALS AND METHODS

A. Test and Control Substances:[ ]Reference/Lot No. 11982-86, was received October 9, 1995. The test substance was a slightly cloudy, colorless liquid and was stored at room temperature in the original container. The Material Safety Data Sheet (MSDS) indicated that the test substance is stable. Records pertaining to the characterization of the bulk test substance were the responsibility of the Sponsor and are maintained at the address indicated for the Sponsor. Residual test substance will be returned to the Sponsor upon completion of the study. Characterization of the 0.9% Sodium Chloride Injection, USP (0.9% saline), positive control substance (1-chloro-2,4-dinitrobenzene; DNCB), Freund's Complete Adjuvant (FCA), and propylene glycol (PG) were provided by the vendors.

B. Dosage Formulations: The following were used to prepare the dosing formulations used in this study: (1) the test substance (TS); (2) FCA (Sigma Immunochemical, St. Louis, MO; Lot No. 084H8800); (3) DNCB (Aldrich Chemical Co., Milwaukee, WI; Lot No. 12423MZ); (4) 0.9% saline (Baxter Healthcare Corp, Deerfield, IL; Lot No. C293399); and (5) PG (J.T. Baker, Inc., Phillipsburg, NJ; Lot No. G48608). In this study, 0.9% saline was used as the vehicle as well as the diluent for FCA. The animals were dosed with one or more of the following formulations: 5% (w/v) TS in 0.9% saline; 75% (w/v) TS in 0.9% saline; undiluted TS; 0.9% saline in FCA (1:1); 5% (w/v) TS in 0.9% saline and FCA (1:1); undiluted 0.9% saline; 5% (w/v) 0.9% saline in FCA and 0.9% saline (1:1), 0.1% DNCB in propylene glycol, 0.1% DNCB in FCA and 0.9% saline (1:1), and undiluted PG. Dosing formulations were prepared at five separate times: (1) for preliminary range-finding studies; (2) for the first (intradermal) induction; (3) for the second (topical) induction; (4) for the first challenge dosing; and (5) for the second challenge dosing. The preliminary rangefinding test evaluated

several concentrations of TS by topical and intradermal application (Appendix 3). Based on the preliminary topical applications, a 5% emulsion was found to be the optimal concentration for the first (intradermal) induction, undiluted (100%) TS for the second induction, and a 75% solution for the challenge.

C. Animals: One hundred sixty (160) male Hartley guinea pigs, approximately 3 weeks of age were received from Sasco, Inc., Madison, WI on November 1, 1995. A random sample (approximately 13%) weighed between 197 and 286 g the following day. Upon arrival, the animals were held in quarantine for approximately three weeks and examined carefully to ensure their health and suitability as test subjects. Guinea pigs selected for the study were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number.

D. Food and Water: Certified Purina Guinea Pig Chow #5026 (PMI Feeds, Inc., St. Louis, MO) and City of Chicago water, supplied by means of an automatic watering system, were available *ad libitum*.

E. Housing and Environment: The guinea pigs were housed individually in stainless steel wire cages measuring 23.9 x 17.8 x 39.8 cm and suspended over excrement pans. Absorbent liners were placed in the pan below the stainless steel mesh floor of each animal cage to absorb liquids. During the treatment phase of the study, the air-conditioned animal room was maintained at a temperature range of 21 to 25°C and a relative humidity range of 51 to 75%. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness.

F. Methods:

1. Animals: Guinea pigs selected for testing were assigned to three groups: a test group of twenty males, a vehicle control group of ten males, and a positive control group of ten males. Group assignments were made using an in-house developed computerized randomization procedure constrained by body weight.

2. Skin Preparation: The guinea pigs were clipped free of hair prior to each induction and before each challenge dose. The animals were also depilated with Neet® Hair Remover (Whitehall Laboratories, Inc., New York, NY) approximately 2 hours before the 24-hour scoring of each challenge.

3. Dosing:

a. First Induction: On November 21, 1995 (Day 1), the fur over the scapula of each animal in an area of approximately 4 x 6 cm was shaved and six intradermal injections (three pairs) of 0.1 ml of the dosing formulations were made flanking the dorsal midline according to the following scheme:

	Test Substance (N = 20)			Vehicle Control (N = 10)			Positive Control (N = 10)	
	(Left)	(Right)		(Left)	(Right)		(Left)	(Right)
1[a]	TS/V[b]	TS/V	1	V	V	1	DNCB/PG	DNCB/PG
2	saline[c]/FCA	saline/FCA	2	saline/FCA	saline/FCA	2	saline/FCA	saline/FCA
3	TS/saline/FCA	TS/saline/FCA	3	V/FCA/saline	V/FCA/saline	3	DNCB/FCA/saline	DNCB/FCA/saline

[a] = site
[b] V = Vehicle (0.9% saline)
[c] saline = 0.9% saline

b. Second Induction: On Day 8 (November 28, 1995), the same region of each animal was again shaved and a 2 x 4 cm Webril® Appli-Pad (Kendall Co., Boston, MA) was saturated (1.5 ml) with neat test substance and applied topically over the six injection sites of each test substance-treated animal. Vehicle control animals were similarly dosed with undiluted vehicle (0.9% saline), while positive control animals were similarly dosed with 0.1% DNCB in PG. The animals were then wrapped with an elastic adhesive bandage (Elastoplast®, Beiersdorf, Inc., Norwalk, CT). All wrapping materials were removed 48 hours after application.

c. First Challenge: On Day 22 (December 12, 1995), two weeks following application of the last induction dose, 0.3 ml of the test substance formulation at a concentration of 75% (w/v) in vehicle (0.9% saline) was applied to the shaved upper left flank and 0.3 ml of undiluted vehicle was applied to the shaved upper right flank of each of the twenty test substance-treated guinea pigs. Vehicle control guinea pigs also received a challenge dose of 0.3 ml of the 75% (w/v) test substance/vehicle formulation applied to the upper left flank and 0.3 ml of undiluted vehicle applied to the upper right flank. Positive control animals received 0.3 ml of 0.1% DNCB/PG applied to the upper left flank and undiluted

(100%) PG applied to the upper right flank. The dosing material for the challenge doses was applied using Hill Top Chambers®, and animals were wrapped with an adhesive bandage (Elastoplast®). All wrapping materials were removed 24 hours after the first challenge dose.

d. Second Challenge: On Day 29 (December 19, 1995), one week following the first challenge dosing, the test substance-treated and vehicle control animals received a second challenge dose. The methods and dosing formulations for the second challenge were identical to those used for the first challenge, except that the Hill Top® chambers were applied to the lower right and left flanks of the animals.

4. Skin Examination: Twenty-four (24) and 48 hours following removal of the wrappings after each challenge dose (Days 24, 25, 31, and 32), the test sites were scored for erythema and edema according to the Draize scale (Appendix 1). To facilitate scoring, all animals were depilated with Neet® Hair Remover (Whitehall Laboratories, Inc., NY) approximately 2 hours prior to each 24-hour scoring.

5. Observations: All guinea pigs were observed daily for mortality and morbidity during the treatment period of the study.

6. Body Weights: Animals were weighed weekly (*i.e.*, prior to dosing on dosing days).

7. Animal Disposition: After the final observation all guinea pigs were euthanized by carbon dioxide asphyxiation and discarded without necropsy.

G. Evaluation: Results obtained from each of the test substance-exposed animals were compared within the test substance group and between the test substance and vehicle control groups. The results of the challenge were expressed in terms of the incidence and severity of the skin response (*i.e.*, erythema and/or edema scores). An incidence index was calculated by dividing the number of animals with responses of a score of 1 or greater at 24 and 48 hours by the number of animals tested. The severity index is the sum of the skin scores divided by the number of animals tested. A comparison of the reactions elicited in terms of incidence, severity, and duration between the vehicle control and treated groups was made to determine whether the test substance induced

sensitization. The test substance was then classified according to its allergic potential using the modified scoring rating of Kligman (Appendix 1).

H. Archives: All original data generated at IITRI and a copy of the final report will be retained in the IITRI Archives (10 W. 35th Street, Chicago, IL, 60616) for five years from the date of this report. At that time, the Sponsor will be contacted in order to determine its final disposition.

III. RESULTS

A. Mortality: No deaths occurred during the study.

B. Skin Effects: A summary of the preliminary topical application erythema scores are presented in Appendix 3. Individual erythema and edema scores after challenge(s) are presented in Appendix 2 and positive scores (*i.e.*, erythema and/or edema response of 1 or greater) are summarized as incidence and severity indices in Table 1. All of the positive control animals exhibited a positive response at the DNCB challenge site, resulting in incidence and severity indices of 100% and 3.25, respectively. Following the first challenge, six of 20 test substance-treated animals exhibited positive responses at the 24-hour scoring and eight exhibited positive responses at the 48-hour scoring, resulting in a combined incidence index of 35% and a combined severity index of 0.50. In the vehicle control group following the first challenge, two of ten animals exhibited positive responses at the 24-hour scoring and none at the 48-hour scoring. This resulted in a combined incidence index of 10% and a combined severity index of 0.10. Since the results of the first challenge dose were inconclusive, a second challenge dose was performed.

Following the second challenge dose, 13 of 20 animals in the test substance-treated group exhibited a positive response at the 24-hour scoring and 19 exhibited a positive response at the 48-hour scoring, resulting in a combined incidence index of 80% and a combined severity index of 1.65. In the vehicle control group following the second challenge, one of ten animals had a positive response at the 24-hour scoring and none at the 48 hour scoring, resulting in a combined incidence index of 5% and a combined severity index of 0.05. Two animals in the test substance-treated group exhibited a positive response

at the vehicle (right flank) challenge site resulting in a combined incidence index of 5% and combined severity index of 0.08. No positive reactions were observed at the same site in the vehicle or positive control-treated animals.

C. Body Weights: A summary of mean body weights is presented in Table 2. All animals gained weight during the study.

IV. EVALUATION

All positive control animals exhibited a positive response (*i.e.*, erythema scores greater than 1) during the study, therefore, the test system was considered valid. A positive response in the test substance-treated animals following the challenge dose resulted in combined (24 and 48 hour) incidence and severity indices of 80 % and 1.65, respectively. According to the modified scoring rating of Kligman[ ]is considered a strong skin sensitizer in guinea pigs.

V. TABLES

SKIN SENSITIZATION STUDY OF[ ]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

TABLE 1

Summary of Incidence and Severity Indices After Challenge

	First Challenge Treated Group		
	24 hours	48 hours	Combined
Incidence[a] index			
Left side	6/20 (30%)	8/20 (40%)	14/40 (35%)
Right side	0/20 (0%)	0/20 (0%)	0/40 (0%)
Severity[b] index			
Left side	9/20 (0.45)	11/20 (0.55)	20/40 (0.50)
Right side	0/20 (0)	0/20 (0)	0/40 (0)

	Vehicle Control Group		
	24 hours	48 hours	Combined
Incidence index			
Left side	2/10 (20%)	0/10 (0%)	2/20 (10%)
Right side	0/10 (0%)	0/10 (0%)	0/20 (0%)
Severity index			
Left side	2/10 (0.20)	0/10 (0)	2/20 (0.10)
Right side	0/10 (0)	0/10 (0)	0/20 (0)

	Positive Control Group		
	24 hours	48 hours	Combined
Incidence index			
Left side	10/10 (100%)	10/10 (100%)	20/20 (100%)
Right side	0/10 (0%)	0/10 (0%)	0/20 (0%)
Severity index			
Left side	33/10 (3.30)	32/10 (3.20)	65/20 (3.25)
Right side	0/10 (0)	0/10 (0)	0/20 (0)

[a] Number of animals showing a positive score (erythema and/or edema response of 1 or greater) at that site ÷ total number of animals in the group x 100
[b] Sum of the erythema scores for the site ÷ total number of animals in the group

SKIN SENSITIZATION STUDY OF [ ]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

TABLE 1 (cont.)

Summary of Incidence and Severity Indices After Challenge

Second Challenge

	Treated Group 24 hours	48 hours	Combined
Incidence[a] index			
Left side	13/20 (65%)	19/20 (95%)	32/40 (80%)
Right side	1/20 (5%)	1/20 (5%)	2/40 (5%)
Severity[b] index			
Left side	19/20 (0.95)	47/20 (2.35)	66/40 (1.65)
Right side	2/20 (0.10)	1/20 (0.05)	3/40 (0.08)

	Vehicle Control Group 24 hours	48 hours	Combined
Incidence index			
Left side	1/10 (10%)	0/10 (0%)	1/20 (5%)
Right side	0/10 (0%)	0/10 (0%)	0/20 (0%)
Severity index			
Left side	1/10 (0.10)	0/10 (0)	1/20 (0.05)
Right side	0/10 (0)	0/10 (0)	0/20 (0)

[a] Number of animals showing a positive score (erythema and/or edema response of 1 or greater) at that site ÷ total number of animals in the group x 100
[b] Sum of the erythema scores for the site ÷ total number of animals in the group

SKIN SENSITIZATION STUDY OF[ ]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

TABLE 2

Summary of Mean Body Weights (g)

		Week 0	Week 1	Week 2	Week 3	Week 4	Gain[a]
Test Substance-Treated	Mean	426	479	520	578	595	170
	Std. Dev.	36.0	37.1	40.8	46.3	45.3	31.8
	N[b]	20	20	20	20	20	20
Vehicle Control	Mean	396	444	487	545	568	172
	Std. Dev.	26.3	23.2	26.7	33.5	39.8	24.2
	N	10	10	10	10	10	10
Positive Control	Mean	403	458	497	567	–[c]	164
	Std. Dev.	35.9	47.0	54.5	64.8	–	40.0
	N	10	10	10	10	–	10

[a] Total Gain = Week 4 - Week 0 for test-substance treated and vehicle control animals; Week 3 - Week 0 for positive control animals
[b] N = number of animals
[c] positive control animals sacrificed on Day 25; no data

VI. APPENDICES

SKIN SENSITIZATION STUDY OF[ ]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

APPENDIX 1

Scale for Scoring Skin Reactions

Evaluation of skin reactions

Erythema and eschar formation:	Score
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Edema formation:	Score
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure)	4

Draize, J.H. Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, Assoc. Food and Drug Officials of the U.S., Austin, Texas, 1959.

Modified Scoring Rating for Allergic Potential

% of Animals Sensitized	Grades	Classification
10	I	Weak
11-30	II	Mild
31-60	III	Moderate
61-80	IV	Strong
81-100	V	Extreme

Kligman, A.M., "J. Invest. Dermatology," 1966.

SKIN SENSITIZATION STUDY OF[ ]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

APPENDIX 2

Individual Erythema and Edema Scores after Challenge

First Challenge

Animal Number	Test Substance Group 24 hr score Left[a]	Right[b]	48 hr score Left[a]	Right[b]	Animal Number	Vehicle Control Group 24 hr score Left[a]	Right[b]	48 hr score Left[a]	Right[b]	Animal Number	Positive Control Group 24 hr score Left[c]	Right[d]	48 hr score Left[c]	Right[d]
910	0/0[e]	0/0	0/0	0/0	930	0/0	0/0	0/0	0/0	940	3/0	0/0	2/0	0/0
911	0/0	0/0	0/0	0/0	931	0/0	0/0	0/0	0/0	941	3/0	0/0	3/0	0/0
912	0/0	0/0	0/0	0/0	932	0/0	0/0	0/0	0/0	942	3/0	0/0	2/0	0/0
913	0/0	0/0	1/0	0/0	933	1/0	0/0	0/0	0/0	943	3/0	0/0	4/0	0/0
914	1/0	0/0	1/0	0/0	934	0/0	0/0	0/0	0/0	944	4/0	0/0	4/0	0/0
915	2/0	0/0	2/0	0/0	935	0/0	0/0	0/0	0/0	945	3/0	0/0	2/0	0/0
916	0/0	0/0	0/0	0/0	936	1/0	0/0	0/0	0/0	946	3/0	0/0	4/0	0/0
917	0/0	0/0	0/0	0/0	937	0/0	0/0	0/0	0/0	947	4/1	0/0	4/0	0/0
918	0/0	0/0	0/0	0/0	938	0/0	0/0	0/0	0/0	948	3/0	0/0	3/0	0/0
919	0/0	0/0	0/0	0/0	939	0/0	0/0	0/0	0/0	949	4/1	0/0	4/0	0/0
920	0/0	0/0	0/0	0/0										
921	2/0	0/0	1/0	0/0										
922	0/0	0/0	0/0	0/0										
923	0/0	0/0	1/0	0/0										
924	2/0	0/0	2/0	0/0										
925	1/0	0/0	2/0	0/0										
926	1/0	0/0	1/0	0/0										
927	0/0	0/0	0/0	0/0										
928	0/0	0/0	0/0	0/0										
929	0/0	0/0	0/0	0/0										

[a] Left = left flank (test substance in vehicle)
[b] Right = right flank (vehicle only)
[c] Left = left flank (DNCB in propylene glycol)
[d] Right = right flank (propylene glycol only)
[e] Erythema/edema score

SKIN SENSITIZATION STUDY OF [redacted]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

APPENDIX 2 (cont.)

Individual Erythema and Edema Scores after Challenge

Second Challenge

Animal Number	Test Substance Group 24 hr score Left[a]	Right[b]	48 hr score Left[a]	Right[b]	Animal Number	Vehicle Control Group 24 hr score Left[a]	Right[b]	48 hr score Left[a]	Right[b]
910	1/0[e]	0/0	2/0	0/0	930	0/0	0/0	0/0	0/0
911	0/0	0/0	1/0	0/0	931	0/0	0/0	0/0	0/0
912	1/0	0/0	3/0	0/0	932	0/0	0/0	0/0	0/0
913	1/0	0/0	3/0	0/0	933	0/0	0/0	0/0	0/0
914	2/0	0/0	3/0	0/0	934	0/0	0/0	0/0	0/0
915	0/0	0/0	3/0	0/0	935	0/0	0/0	0/0	0/0
916	1/0	0/0	2/0	0/0	936	1/0	0/0	0/0	0/0
917	0/0	0/0	1/0	0/0	937	0/0	0/0	0/0	0/0
918	1/0	0/0	3/0	0/0	938	0/0	0/0	0/0	0/0
919	2/0	0/0	4/0	0/0	939	0/0	0/0	0/0	0/0
920	1/0	0/0	2/0	0/0					
921	1/0	0/0	2/0	0/0					
922	1/0	0/0	2/0	0/0					
923	0/0	0/0	2/0	1/0					
924	1/0	0/0	3/0	0/0					
925	2/0	2/0	3/0	0/0					
926	3/0	0/0	4/0	0/0					
927	0/0	0/0	0/0	0/0					
928	0/0	0/0	1/0	0/0					
929	2/0	0/0	3/0	0/0					

[a] Left = left flank (test substance in vehicle)
[b] Right = right flank (vehicle only)
[c] Left = left flank (DNCB in propylene glycol)
[d] Right = right flank (propylene glycol only)
[e] Erythema/edema score

SKIN SENSITIZATION STUDY OF [ ]
USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

APPENDIX 3

Summary of Preliminary Testing (Topical)

Temporary Animal No.	Test Substance Concentration (w/v)	Vehicle	Erythema Score 24 hr	Erythema Score 48 hr
562	100%	–	1	0
	75%	0.9% saline	0	0
	50%	0.9% saline	0	0
	25%	0.9% saline	0	0
565	100%	–	1	0
	75%	0.9% saline	0	0
	50%	0.9% saline	0	0
	25%	0.9% saline	0	0